

Investigating infertile couples

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Objectives:



Identify the causes of infertility in men and women.



Understand the diagnostic approaches to infertility in men and women.



Interpret the results of investigation of infertility in men and women.

Overview:



Infertility / subfertility



Clinical history and physical examination



Endocrine investigations in subfertile women



Endocrine causes of female infertility



Endocrine investigations in subfertile men



Diagnostic approaches to subfertility in women and men



Hyperprolactinemia



Infertility is an absolute inability to conceive, but most of the causes are relative/due to secondary causes, so we call it subfertility.

Infertility/Subfertility (Not Absolute Ability to conceive)

Definition	<p>Failure of a couple to conceive after one year of regular, unprotected intercourse.</p> <ul style="list-style-type: none"> • Age associated especially in female (Ovarian Reserve) • >35 start investigation after 6 months • <35 + frequent intercourses = start investigating after 1 year 	
Causes	<p>Endocrine: Common in females (1/3 patients) & rare in males. 1/3 Both, 1/3 male and Idiopathic</p> <p>Idiopathic: In some couples no cause can be identified idiopathic</p> <p>Hormone dysfunction is a rare cause of male infertility</p>	
Causes	<ol style="list-style-type: none"> 1. Quantity and quality of : <ul style="list-style-type: none"> ◦ Ovum (oocyte) ◦ Sperm 2. Site (of fertilization) 	
Clinical history		Physical examination
<p>Information on clinical history of the patient should include:</p> <ol style="list-style-type: none"> 1. Previous pregnancies secondary Infertility 2. Use of contraceptives especially the oral, will cause anovulation in first few cycles after stopping 3. Serious illness 4. Past chemo/radiotherapy damage the oocyte 5. Congenital abnormalities 6. Drug usage 7. STDs (Sexually Transmitted Diseases) e.g. chlamydia 8. Frequency of intercourse semen Fertilize up to 5 days 		<p>Information on physical examination of the patient should include :</p> <ol style="list-style-type: none"> 1. Hypothalamic-pituitary, thyroid disorders Goiter, Exophthalmus 2. Cushing syndrome Central obesity, purple stria 3. Galactorrhea (Lactation in the absence of pregnancy, most commonly due to hyperprolactinemia) 4. Hirsutism <p>↑BMI (Android pattern of obesity)→Insulin resistance → ↑Androgens</p>

Endocrine investigations in subfertile women

- Investigations are based on the phase of menstrual cycle (Regularity)+(association with the normal symptoms of ovulation)
- Serum progesterone should be measured in the **middle of the luteal phase (day 21)**. Reaches the peak after 1 week of Luteal phase
- High progesterone (>30 nmol/L) indicates ovulation. If it less than 10 it indicates anovulation
- In oligomenorrhea ≤8 cycles in 1 year or amenorrhea absence of menstrual cycles for 6 months hormone measurement is needed.

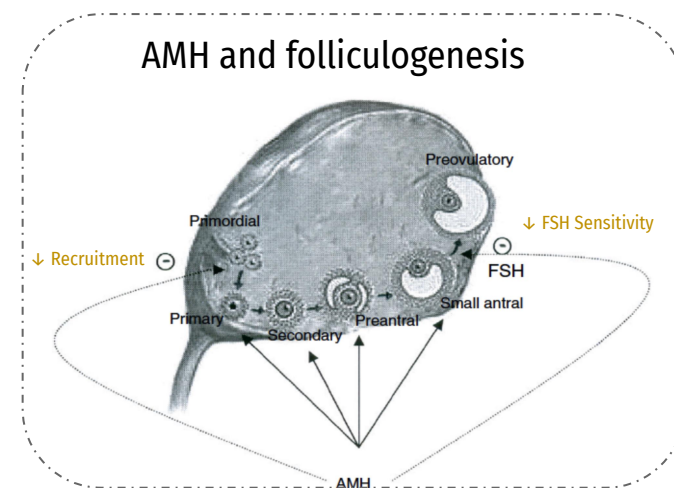
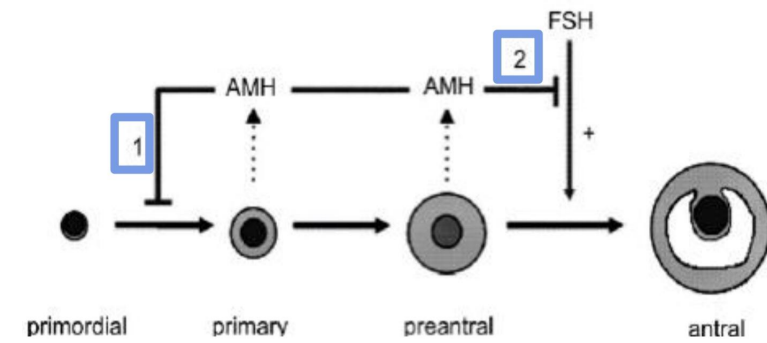
Endocrine causes of female infertility:

1. Excessive secretion of ovarian androgens..E.g. Obesity ↓SHBG = ↑free testosterone & Insulin resistance.
2. Cushing's syndrome ↑cortisol = ↑Androgens
3. Primary ovarian failure: low oestradiol (postmenopausal hormonal pattern) will lead to high gonadotropins, in this case hormone replacement therapy can be given but it will **NOT** treat infertility. Helps with libido
4. Hyperprolactinemia
5. PCOS (PolyCystic Ovary Syndrome) associated with insulin resistance
6. Hypogonadotropic hypogonadism: Low gonadotropins, low oestradiol, it's due to hypothalamic-pituitary lesion & it's rare.

Anti mullerian hormone (AMH)

- Stop the development of female genitalia (tubes) in male
- Start to secrete by the age of puberty

- ❖ It's a polypeptide hormone called **Mullerian-inhibiting substance**, it's secreted by the growing (immature) ovarian follicles and the secretion is proportional to follicular development. **Young woman = ↑AMH**
- ❖ **Function:** It prevents the premature depletion of follicles. Thus, its measurement helps in assessing the ovarian reserve and female fertility.
- ❖ **Predict starting of menopause**
- ❖ **Ovarian reserve:** number and quality of oocytes in the ovaries. (**Primordial follicles**)



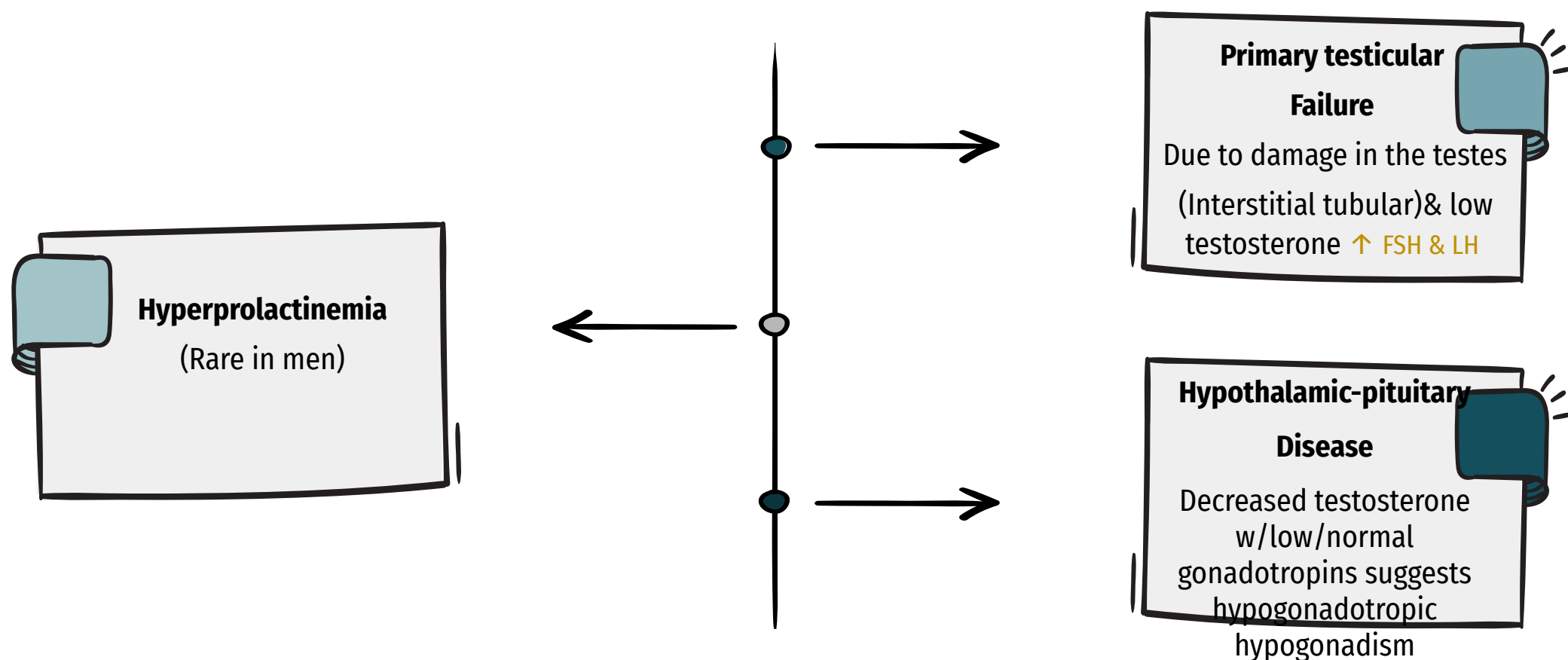
- 1 AMH in the ovary will **inhibit** the initial recruitment of primary follicles from primordial follicles. **Prevent premature depletion of follicles**
 - 2 AMH In the ovary will **inhibit** the sensitivity of antral follicles to **FSH** during cyclical recruitment. **Preventing it from becoming oocyte**
- ★ The number of remaining primordial follicles correlate with the number of growing follicles. Since **only** growing follicles produce AMH, its plasma levels reflect the number of remaining primordial follicles.

Endocrine investigations in subfertile men

Eugonadal men with normal sperm analysis do not require endocrine investigations, while in hypogonadal men the testosterone hormone and gonadotropins should be measured.

Semen analysis: sample collection should be done 48-72 hr of abstinence
 Volume **at least 1.5 ml**, liquefaction time **20-30 min**, sperm count **at least 15 millions sperms/ml**, if less than that it is termed as oligospermia motility **<32%**
 presence of abnormal spermatozoa, PH (should be 7.2-7.8, acidity damage the sperm), WBCs

Causes of male infertility



Diagnostic approach to Subfertility

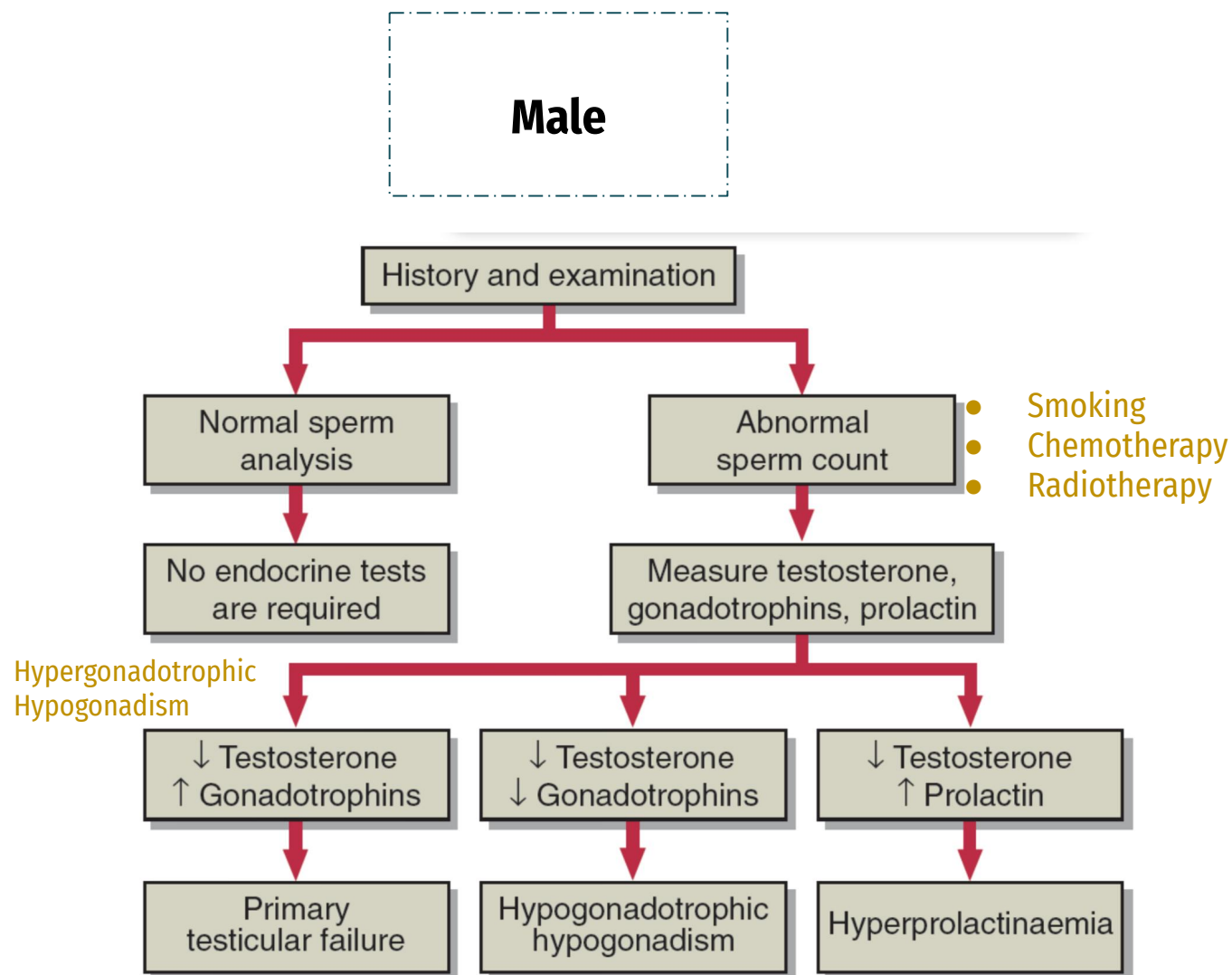


Fig 51.2 Diagnostic approach to subfertility in the man.

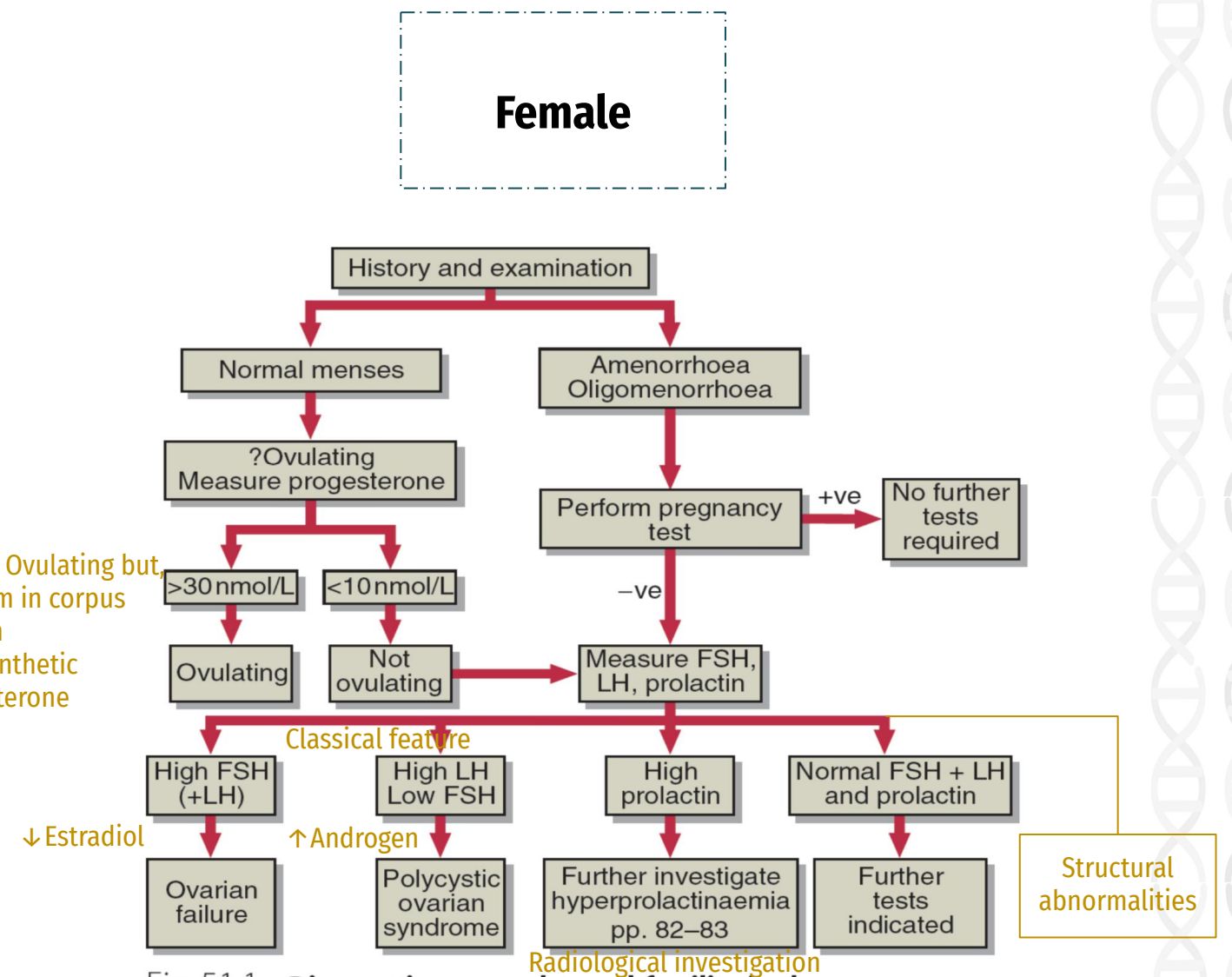


Fig 51.1 Diagnostic approach to subfertility in the woman.

Hyperprolactinemia	
Hormone affected	Prolactin: it's an anterior pituitary hormone.
Regulation	Its secretion is tightly regulated by: TRH (Stimulation), Dopamine (Inhibition) both from hypothalamus. e.g. antidepressants
Target	It acts directly on the mammary glands to control lactation
Abnormal secretion	Elevation → Causes infertility in both sexes due to gonadal function impairment.
Early indication	- In women: amenorrhea & galactorrhea. - In men: none. Adenoma → compress optic nerve → vision disturbance and headache
Diagnosis	Exclude the following: - Stress. - Drugs. - Other diseases. Differential diagnosis: - Prolactinoma. MRI can be done - Idiopathic hypersecretion. Give dose of TRH and check the prolactin level / check the dopamine level
Causes	<ol style="list-style-type: none"> 1. Stress. 2. Primary hypothyroidism (↑ TRH → ↑ prolactin) & other pituitary disease. 3. Prolactinoma. 4. Drugs (estrogens, phenothiazines, metoclopramide, α-methyl dopa). 5. Seizures. 6. Idiopathic hypersecretion (e.g. impaired secretion of dopamine). 7. Pituitary diseases

Take Home Messages



Endocrine causes of infertility are more common in women than men & Hyperprolactinemia is a rare cause of male infertility.



In women serum progesterone >30 nmol/L indicates ovulation.

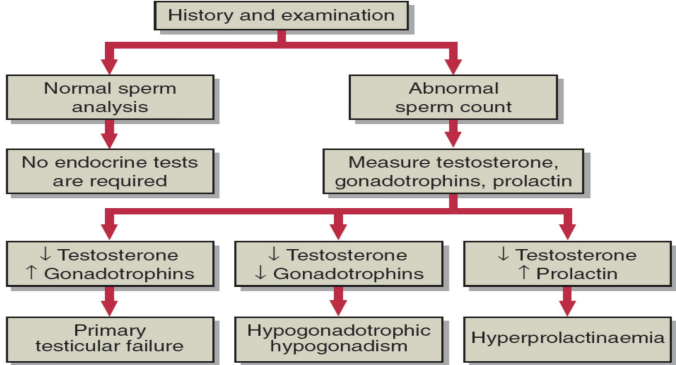
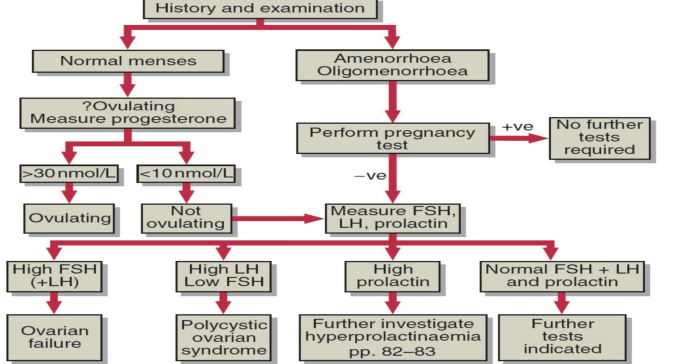


When you realize only Allah can defeat Thanos.



Ramadan Kareem

Summary

Infertility in females	Endocrine Investigations	<ul style="list-style-type: none"> Investigations are based on the phase of menstrual cycle Serum progesterone should be measured in the middle of the luteal phase (day 21) High progesterone (>30 nmol/L) indicates ovulation. In oligomenorrhea or amenorrhea, hormone measurement is needed.
	Anti mullerian hormone (AMH)	<ul style="list-style-type: none"> It's a polypeptide hormone called Mullerian-inhibiting substance, it's secreted by the growing (immature) ovarian follicles and the secretion is proportional to follicular development. Function: It prevents the premature depletion of follicles. Thus, its measurement helps in assessing the ovarian reserve and female fertility. Ovarian reserve: number and quality of oocytes in the ovaries.
	Causes	<p>Infertility is caused by:</p> <ul style="list-style-type: none"> Primary ovarian failure : ↑ LH / ↑ FSH / ↓ Progesterone. PCOS : ↑ LH / ↓ FSH / ↓ Progesterone. Hyperprolactinemia : ↑ Prolactin / ↓ LH / ↓ FSH / ↓ Progesterone. Cushing's syndrome. Hypogonadotropic hypogonadism . Excessive secretion of ovarian androgens (obesity).
Infertility in males	Endocrine Investigations	<ul style="list-style-type: none"> Eugonadal men with normal semen analysis (such as pH, volume, motility and sperm count) do not require endocrine investigations.
	Causes	<p>Infertility is caused by:</p> <ul style="list-style-type: none"> Endocrine cause of infertility in men are rare. Primary testicular failure: ↑ Gonadotropins / ↓ Testosterone. hypogonadotropic hypogonadism : ↓ Gonadotropins / ↓ Testosterone. Hyperprolactinemia (rare): ↑ Prolactin / ↓ Testosterone.
Diagnostic approach to Subfertility	Male	 <p>Fig 51.2 Diagnostic approach to subfertility in the man.</p>
	Female	 <p>Fig 51.1 Diagnostic approach to subfertility in the woman.</p>
Hyperprolactinemia	Regulation	<ul style="list-style-type: none"> Secretion of prolactin is regulated by TRH (stimulation) and dopamine (inhibition).
	Abnormal Secretion	<ul style="list-style-type: none"> Elevated circulating prolactin causes infertility in both sexes due to gonadal function impairment, early indication in women is amenorrhea/galactorrhea.
	Causes	<p>It's caused by:</p> <ul style="list-style-type: none"> Stress seizures drugs (estrogens, phenothiazines, metoclopramide, α-methyl dopa) Primary hypothyroidism. Prolactinoma. Idiopathic hypersecretion.



MCQs

1- Which of the following drugs could cause hyperprolactinemia?

A-Bromocriptine	B-Cabergoline	C-Metoclopramide	D-Cycloset
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2- Which of the following is FALSE about primary ovarian failure?

A-Low gonadotropins	B-It follows a postmenopausal hormonal pattern	C- Low oestradiol	D-Infertility cannot be treated by HRT
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3-Progesterone should be measured in which phase?

A-Ovulation phase (Day 21)	B- Ovulation phase (Day 28)	C-Luteal phase (Day 21)	D-Luteal phase (Day 28)
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4-Which of the following is TRUE about AMH?

A-It stimulates the initial recruitment of primary follicles	B- Its plasma levels reflect the number of remaining primordial follicles	C-It inhibits the sensitivity of antral follicles to LH	D-None
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5- Which of the following is TRUE in primary testicular failure?

A- ↓ Testosterone ↑ prolactin	B- ↓ Testosterone ↑ Gonadotropins	C- ↓ Testosterone ↓ Gonadotropins	D- ↑ Testosterone ↑ Gonadotropins
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6-In polycystic ovarian syndrome, which hormone is elevated?

A-Dopamin	B- Progesterone	C-FSH	D-LH
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Answers key

1- C 2- A 3- C 4- B 5- B 6- D



SAQs

1- List 3 information that should be included in the physical examination of infertility and 3 in the clinical history?

Answer :

Physical Examination: Cushing's syndrome - Hirsutism - Galactorrhea.

Clinical History: Previous pregnancy - Use of drugs - Chemotherapy.

2- List 3 causes of infertility in females and 3 in males?

Answer :

Females: Primary ovarian failure - PCOS - Hyperprolactinemia

Males: Primary testicular failure - Hypogonadotropic hypogonadism - Hyperprolactinemia

3- List 4 causes of hyperprolactinemia?

Answer:

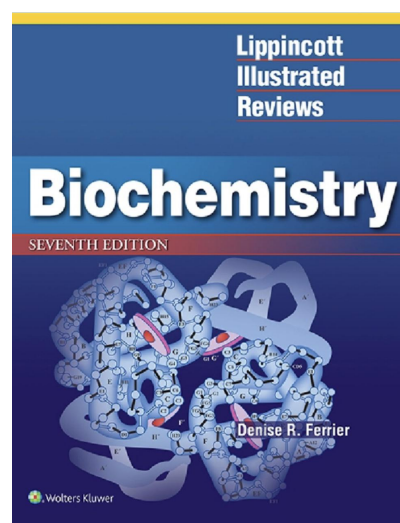
Prolactinoma - Stress - Drugs such estrogens - Primary hypothyroidism

4-List 2 actions of AMH on the ovary?

Answer:

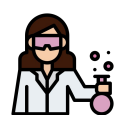
In the ovary it will inhibits both the initial recruitment of primary follicles from primordial follicles and the sensitivity of antral follicles to FSH during cyclical recruitment.

Resources Click on the book to download the resource





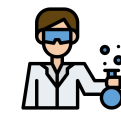
Leaders



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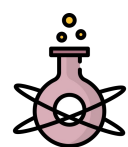


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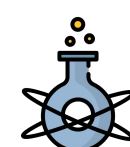
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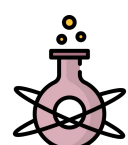


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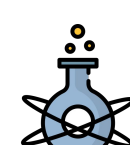
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Mubarak Alanazi

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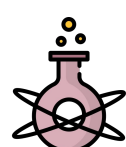


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Special thanks to Fahad AlAjmi for designing our team's logo.